Potassium & sodium disorders

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Potassium is the main electrolyte inside the cell, while the sodium is the main electrolyte outside the cell.
Na^+ concentration is 140 mmol/L outside the cell, & K+ concentration is 140 mmol/L inside the cell.
Potassium disorders are either hypokalemia or hyperkalemia

($\downarrow K^+$) HYPOKALEMIA ($\downarrow K^+$)

Definition :

When the Serum concentration of K^+ is < 3.5 mmol/L , we call it hypokalemia

In epidemiological studies, it has been shown that it happens In 20-50% of **thiazide users**

NB

Thiazide:

- A diuretic work on distal tubules & has some side effect e.g. hyperglycemia & hyperuremia but the main one is hypokalemia

Loop diuretic, *such as furosemide "lasix" which has less side effect*, if used more than once/day $\Rightarrow$ relatively more severe hypokalemia

Etiology:

It can happen either:

1- With normal total body K^+ $\Rightarrow$ intracellular shift (*shift from outside the cell to inside the cell*).

NB

The total K+ concentration inside the cells is 3400 mmol & 60 mmol outside cells (plasma & interstitium).
So, the total K^+ is 3460, and if this 3460 is not decreased but the serum conc. decreased, it will shifted from extracellular to intracellular space.

2- Or with depletion of total body K^+: ether by

↑ Renal excretion (renal loss)

↑ GI excretion (GI loss)

↓ K^+ intake (starvation, anorexia nervosa & prolonged fasting)

Clinical Manifestation:

The symptoms of hypokalemia are **mainly muscular** (neuromuscular junction), while in hyperkalemia it is mainly **on the heart**.

- Neuromuscular: Motor weakness, paralysis, fever, constipation, rhabdomyolysis , paralytic ilieus
- Cardiovascular: Digoxin toxicity $\Rightarrow$ *arrhythmia u-waves in ECG.*

Very sever, try to prevent hypokalemia as much as possible in pt. whose taking digoxin.

- Renal: Hypokalemic nephropathy

Proximal tubule vacuolization, interstitial fibrosis/inflammation.

- Metabolic Alkalosis:

Instead of K^+ exchange with Na^+, there will be exchange of H^+ with Na^+, leading to alkalosis.

- Renal concentrating defect:

The kidney will lose its ability to concentrate the urine

- ↑Ammonia production:

To spare the H^+ that loss in the renal tubule.
Precipitating to hepatic encephalopathy.

NB

Precipitating factors to hepatic encephalopathy:
- Constipation, protein diet, GI bleeding, infection, dehydration & electrolyte imbalance (mainly hypokalemia)

ECG Changes with Serum K^+ Levels:

	$[K^+]$ (mmol/L)		
↓K^+	< 3.5		Flattened T-wave + U-wave
HYPERKALEMIA	5 – 6.5		Peaked T-wave
	7 – 8		Widened QRS + (peaked T-wave)
	8 – 9		Sin Wave

Differential Diagnosis of Hypokalemia:

Try to Exclude 1st & 2nd type:

1. **Factitious hypokalemia (Pseudohypokalemia):**
   - Lab. error:
     - » Not all hypokalemia is because of lab error, but if the pt looks well and doesn't has any symptoms of hypokalemia, then take another sample.
   - Severely elevated WBC (>50×10^9/L) [Normal level 4-11×10^9/L]
     - » e.g. leukemia
     - » ↑K^+ uptake by leukemia cells when blood is stored at room temperature for more than ONE hour.

2. **Hypokalemia 2° to intracellullar shift (to inside the cell):**
   - Catecholamine excess:
     - Stress of illness.
     - Exogenous catecholamines (*as in ICU patients whose haemodynamically unstable*):
       - v.v blood pressure
       - Inhaled B. agonist
     - Correction of D.M by insulin (*lead to influx of K^+ inside the cell*)
     - Hypokalemic periodic paralysis : either
       - Primary (idiopathic) or,
       - Secondary to hyperthyroidism
   - Treatment of megaloblatic anemia with B_{12} & folate:
     - » Because there will be new cell formation which lead to ↑K^+ utilization in the newly formed cells
   - Ingestion of soluble barium salt:
     - » Used as contrast of GI X-rays.
     - » When it ingested, it may lead to bonding of K^+ at intestinal cell.

3. True Hypokalemia (decreased total body K^+): By

- Renal losses
- Extra renal losses *(GI losses)*
- Starvation
- → Urine K^+

True Hypokalemia :

Don't forget to ask about **urine K^+** when you have hypokalemia.

- **Extra Renal Losses (Urinary K^+< 30mmol/L):**
  - Diarrhea (*which leads to acidosis*) and Cathartic abuse
  - K^+ binding in the bowel:
    - » Clay Ingestion [أكل الطين]: *lead to exchange of K^+ by Ca^{++} or other minerals.*
  - Villous Adenoma:
    - » It is a cause of diarrhea, but rather than causing acidosis, it causes **alkalosis**
  - Congenital Chloride – losing Diarrhea
  - Cutaneous losses – Burns
- **Renal Losses (urinary K+ > 30mmol/L):**
  - With Metabolic acidosis (↓ Serum HCO_3) : *Check the anion gap*
    - With Normal Anion Gap (AG) :
      - Renal Tubular Acidosis "RTA" (I or II) :
        - » The most common cause.
      - Use of Carbonic Anhydrate Inhibitor [acetazolamide]:

NB

Acetazolamide:

- Work in proximal tubules, week diuretics, the only one causing acidosis, it also can cause alkalosis. It is not usually used in medicine, it is commonly used by ophthalmologist to treat glaucoma.

      - Ureterosigmoidostomy:
        - » After removing the bladder with TTC, the surgeon make a shunt between the ureter and the sigmoid colon, which leads to loss of K^+ and acidosis.

- With High Anion Gap:
  - Diabetic or alcoholic ketoacidosis:
    - » Renal losses 2° to glucosemia "osmotic duresis"

- With Normal pH (rare):
  - Recovery from ATN.
  - Post obstructive duireris.
  - Cisplatin therapy. *(to treat cancer)*
  - Mg^{++} depletion.

- With Metabolic alkalosis (↑ Serum HCO_3): **Most Important**

  Check Urine Chloride:
  - Low $[Cl^-]$ (<10mmol/L) ⇒ Volume depletion (*give him normal saline)*
  - High $[Cl^-]$ (>30mmol/L) ⇒ *Check Blood Pressure*:
    - With Normal BP :
      - Diuretics.
      - Bartter's syndrome.
      - Gitelman's syndrome.

Bartter's VS Gitelman's:
- Both can cause hypokalemia & hypomagenesemia.
- Both have the same clinical presentation with hypokalemia, renal loss and alkalosis and low magnesium, but the mechanism is different.
- Bartter's works as lasix, while Gitelman's works as thiazaide.
- *For more information*: Kumar 6e page (704-706)
  http://www.emedicine.com/MED/topic213.htm

    - With High BP : (↑ in mineral corticord activity)
      - Primary aldosteronism (Conn's)
      - Secondary aldosteronism (RAS)
      - Liddle syndrome :
        - 1963 Alabama, Autosomal dominant.
        - *In collecting duct the Na^+ channal will be active leading increase entry of Na^+ which lead to hypertension and hypokalemia.*
      - Cushing's syndrome (11B, 17d Hydroxylase diff)

(↑K^+) HYPERKALEMIA (↑K^+)

When the Serum K^+ levels is more than **5.5 mmol/L**, we call it hyperkalemia

As the GFR decreases, there is an adaptation by the remaining nephrons with increased K^+ secretion as a result; a normal serum K^+ is generally maintained until the GFR is <20ml/min

Clinical manifestations: *the main effect of hyperkalemia is on the heart*

- Cardiovascular:
  - Arrhythmic including sudden death.
  - Peaked T. Waves.
  - Widened QRS.
- Neuromuscular:
  - Paresthesia.
  - Weakness, Paralysis.
- Renal:
  - Natriuresis (loss of Na+)
  - **↓ ammonia production** :
    - » *Opposite to hypokalemia which leads to Increase ammonia production.*

Work-up of Hyperkalemia (Differential diagnosis):

Try to roll out

1. **Factitious hyperkalemia (Pseudohyperkalemia):**
   - Hemolysis:
     - » *Because of K^+ inside cells, and the lab will till you that the sample get lysed.*
   - Elevation of platelets count to >1000x10^9/L (>1,000,000/dl)
     - » *It is rare but an important cause of hyperkalemia, there is a disease called **Essential thrombocythemia** affecting elderly pts, in which the pt get high platelet count and spleenomegaly with hyperkalemia.*
   - Elevation of WBC to >50,000/dl
     - » *As it causes hypokalemia, it also can cause hyperkalemia.*

2. Shift of K^+ from cells :

- Acidosis:
  - » *Opposite to alkalosis, which lead to shifting of K^+ into cells.*
- Lack of Insulin:
  - » *Diabetic pts, because insulin facilitate entering of K^+ into cells.*
- β blockers
  - » *Propranolol, timolol, etc, all of them cause hyperkalemia.*
- Digoxin intoxication
- Hyperkalemic periodic paralysis (Aut. dominant)

After excluding shifting causes, then think in:

3. Increased of total body K^+:(True Hyperkalemia):

- Increased K^+ intake: *(like banana ,dates & citrates)*
- Impaired renal excretion: *Check GFR*

a. **GFR <20ml/min** ⇒ increased K^+ load:

- Exogeneous source:
  - Dietary intake
  - Salt Substitute
    - » *Some pts with hypertension instead of eating NaCl they eat KCl.*
- Endogeneous source:
  - Hemolysis *(hemolytic anemia)*
  - Rhabdomyolosis *(in burns, statins & trauma)*
  - GI bleeding *(endogenous source of K^+)*
  - β blockers
  - Acidosis

Drugs impairing K+ secretion:

- Spironolactone *(block aldosterone action).*
- Amiloride *(block the apical Na^+ channels in collecting ducts)*
- Triamterne *(both of them K+ sparing)*
- ACE I + I
- Trimethoprim *(block Na^+ channels)* & Cotrimoxazole.
- Heparin ⇒ decrease aldosterone synthesis *(block production of aldesteron in adernal cortex by chronic use)*

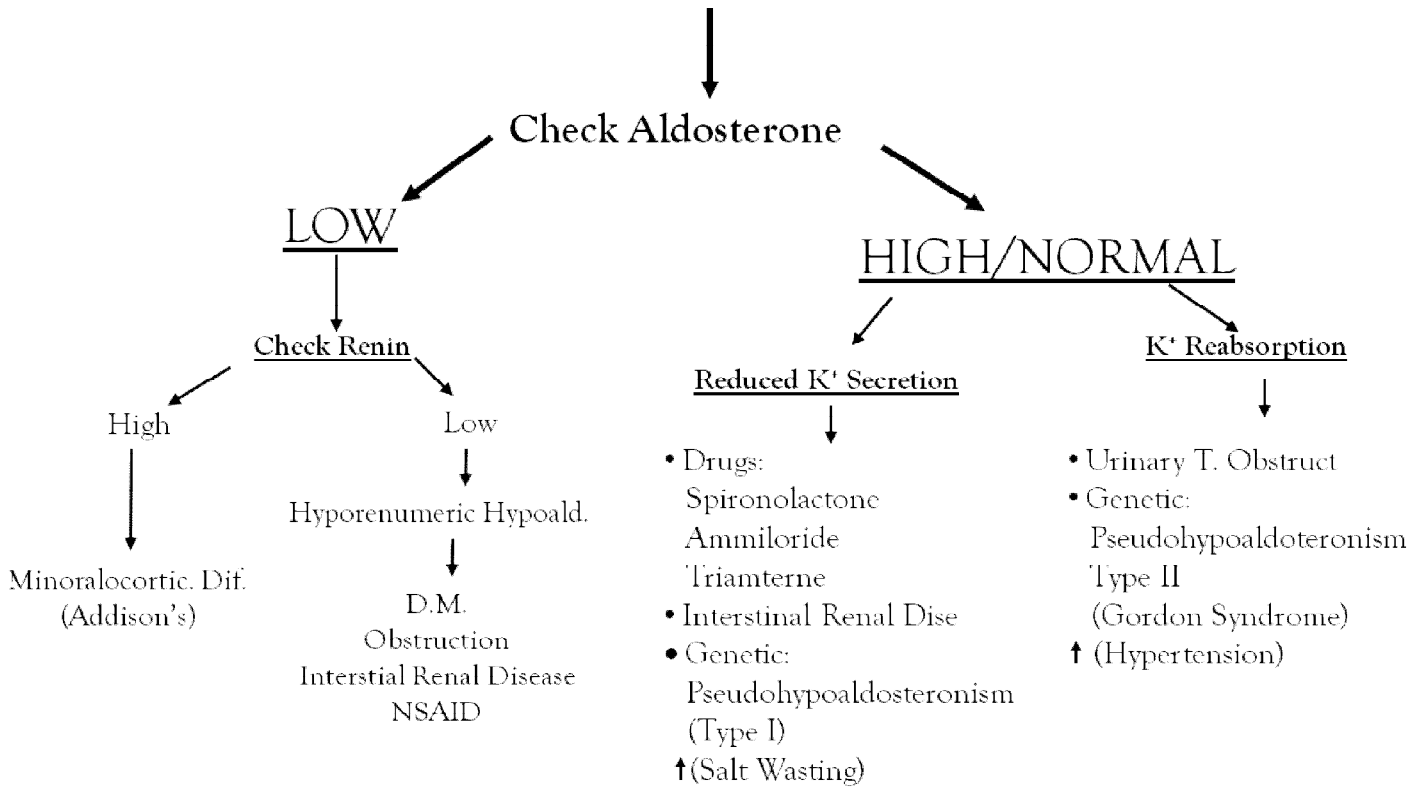
b. **GFR > 20ml/min :**

» *Usually if the GFR is normal, the K^+ will be maintained **Exept** in case of low aldosterone witch is the maintaining mechanism of it.*

- Hyperkalemia secondary to aldosterone dysfunction:

» *Either deficiency or resistance.*

If there is Hyperkalemia with relatively well preserved renal function (GFR > 20ml/min)



Transtubular K^+ Gradient (TTKG):

TTKG is: a measurement of net K^+ secretion by the distal nephron and used to determine if hyperkalemia is caused by aldosterone deficiency/resistance or if the hyperkalemia is 2^O to non-renal causes.

In brief: net K^+ secretion at distal nephron.

$$TTKG = \frac{K\,u \times S\,osm}{K\,s \times U\,osm}$$

K u = K^+ concentration in urine
S osm = Serum osmolarty
K s = K^+ concentation in serum
U osm= Urine osmolarity

TTKG Value	Indication
6 –12	Normal
>10	Suggests normal aldosteron action and an extra renal cause of hyperkalemia
<5–7	Suggests aldosterone deficiency or resistance
After 0.05mg fludrocortisome *(aldesteron synthetics work in distal tubules)*	
>10	Hypoaldosteronism is likely
<10	Aldosterone resistance

If there is no change in TTKG : Suggests a renal tubular defect from either:

- K^+ sparing diuretics (spironolactone, amiloride, triamterne)
- Aldosterone resistance
  - Interstitial kidney disease
  - Pseudohypoaldosteronism type I
- Increased dietal K^+ reabsorption
  - Urinary tract obstruction
  - Pseudohypoaldosteronism type II (Gordon syndrome)

TREATMENT :

Hypokhalemia :

Give patient **KCl** in general but in certain condition (e.g. bartter's disease) *need amoliride or cortisone* .

Hyperkalemia : *v. Important*

1. **Ca gluconate** : to protect heart from arrhythmia 10cc injection (membrane stabilizer) over 5 min
2. **Insulin**: *to reduce K^+ rapidly, lead to shifting of K^+* ,10 units regular insulin, infusion over 20 min. + 50ml glucose 50% dextrose by infusion 10 min.
3. **$NaHCO_3^-$** :but **NOT USED** in CHF, pulmonary edema and hypertension.
4. **β agonist nebulizer** :e.g salbutamol, rapid effect, used nowadays, can be repeated

2,3&4: will lead to K^+ shifting, but after 2 hours, K^+ will return back to blood.
So, we need to give drugs that lead to decrease the K^+ for long period as :

5. **Risins** : They take K^+ & give Ca^{++} or Na^+ in intestinal cell, then they remove it.
   They can be taking orally or rectally (longer time)

If all failed, then we have to do :

6. **Dialysis** : whish is the last thing.

SODIUM DISORDERS :

Na^+ is the main electrolyte extracellularly.

Serum sodium level is a useful clinical index for evaluating water balance, not sodium balance.

Water balance is regulated by:

1. Thirst
2. Antidiuretic hormone (ADH):
   - *Produced by hypothalamus & stored in the post. Pituitary & working in the collecting ducts in special ducts called* **aquaporine**.
3. Renal medullary concentration ability

Serum Osmolality = 2×Na conc.(most important) + glucose + urea

NB

- Na^+ is the main element in the osmolalty, hence its conc. is 140 when multiplied by 2 become 280. So, any change in Na^+ conc. cause a major change in osmolalty.
- Glucose is about 5 and urea is also about 5. So it has minor role in it.
- For example: 280+5+5=290 mmol/L

(↓Na^+) HYPONATREMIA (↓Na^+)

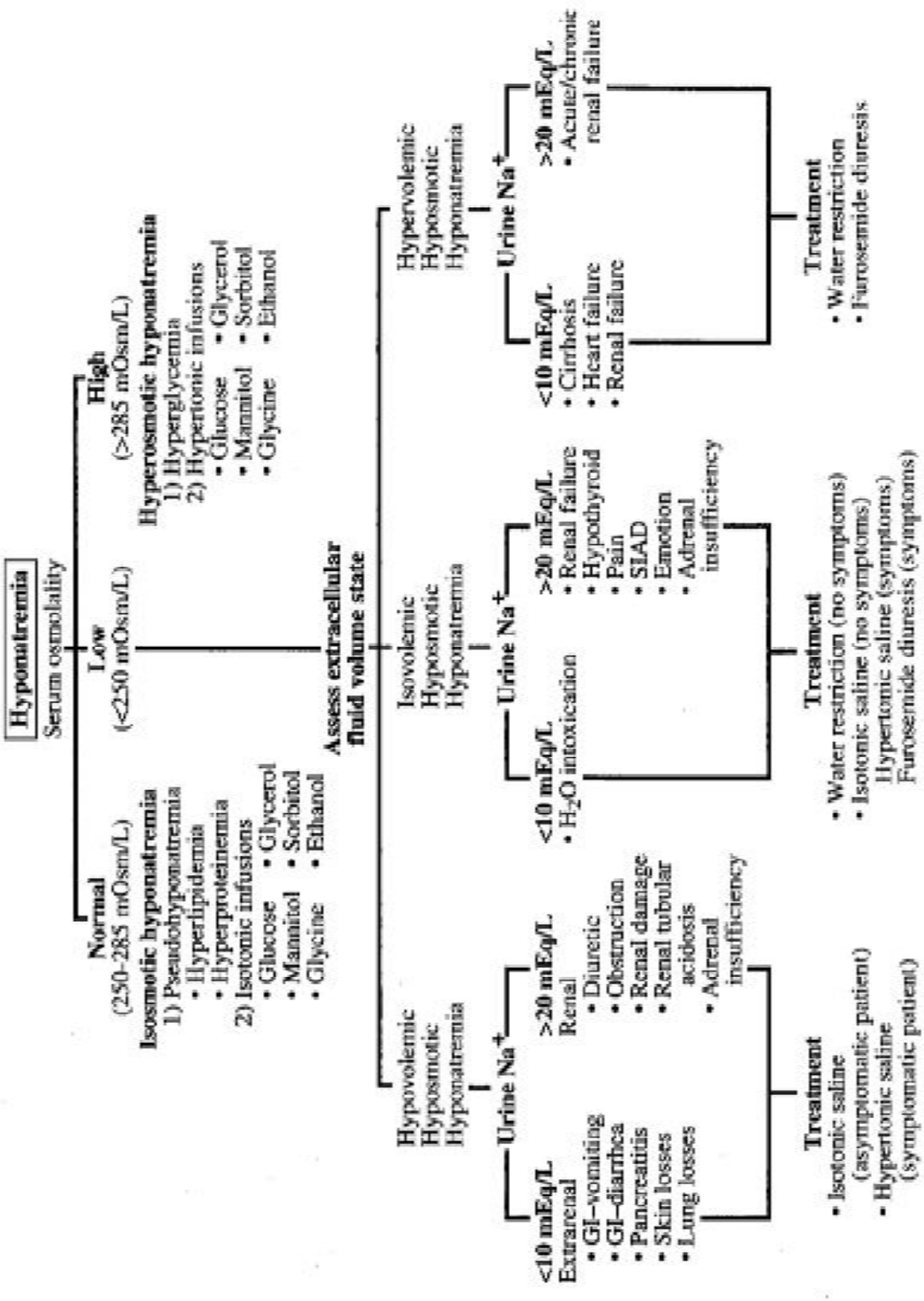
It is the most common electrolyte abnormality in hospitalized patients

Clinical features:

CNS symptoms happen with acute hyponatremia not chronic :

1. Lethargy
2. Cramps
3. Decreased deep tendon
4. Seizures

Diagnosis and Management :



DIFFERENTIATE BETWEEN DIFFERENT TYPES OF HYPONATREMIA:

At first when you have hyponatremia look at osmolarty, is it normal or high or low.

If the osmolarty is normal, it is pseudohyponatremia, which happen in case of hyperlipidemia & hyperprotinemia.

If the osmolarty is high, it could be because of hyperglycemia, because in the equation above, if you have less Na^+ and increase in osmolarty, the glucose must be high.

There is a relation between hyperglycemia and hyponatremia with unknown cause but the relation is when there is an **increase in glucose by 10 mmol above normal it will lead to decrease in Na^+ by 3 mmol**, and if you treat hyperglycemia, Na^+ will return to normal.

Other causes of hyponatremia with high osmolarity, could be because of hypertonic fluid infusion, most commonly mannitol, or if the pt is taking ethanol, or glycine.

- **Glycine**: is an amino acid, it is used in urology & obstetrics.
- In urology, it used in TURP (transurethral prostate resection).
- In obstetrics, it is used in D&C "cleaning the uterus after missed abortion" (transvaginal resection).
- Because they use electrical current to cut, they put the laparoscope in a fluid to suction the blood, they put glycine to prevent electrolyte separation and heat production.
- After these surgeries, glycine go inside the blood which is hypertonic lead to extracellular shift leads to delusional hyponatremia, and they usually order urea and electrolyte after the surgery to treat it.

The true hyponatremia happens when there is decrease in Na^+ and osmolarty (less than 250) hypoosmolar hyponatremia.

In this case you have to look to the volume status, if he has edema, look at the JVP or if he is in the ICU, look at the central venous pressure, and try to determine, is the pt is hypovolemic, isovolemic or hypervolemic.

If the pt is hypovolemic, measure the Na^+ in the urine. If it is low (less than 10), it means that it is extraurinary loss (E.g. diarrhea, vomiting, pancreatitis, burns).

If it is high (more than 20), it means that it is an urinary loss through the kidney (e.g. diuretics, etc.) and the treatment is just to give normal saline.

If the pt is hypervolemic hypoosmotic hyponatremic , its causes are liver cirrhosis, heart failure and renal failure. Its treatment is by fluid restriction & diuretics.

If the pt is euvolemic, which is the most dangerous one , has 3 main causes which are , SIAD, hypothyroidism & glucocorticoid deficiency.

SIAD : [syndrome of inappropriate **antidiuresis**]

- Has recently replaced the previous term : SIADH [syndrome of inappropriate **antidiuretic hormone**] because up to 20% of patients who fulfill the criteria for SIAD do not have detectable circulating levels of antidiuretic hormone.
- It is a diagnosis of exclusion

Criteria for the diagnosis of SIAD :

1. Hypotonic plasma.
2. Urine osmolality is greater than serum osmolality (or >100 – 150 mOsm/kg).
3. Urine sodium matches intake.
4. Absence of hypoadrenalism and hypothyroidism.
5. Improvement with water restriction.

Important clues:

Low serum levels of :
- Uric acid
- BUN
- Creatinine

Causes of SIAD :

Causes of the syndrome of inappropriate vasopressin secretion

Carcinomas	Pulmonary disorders	Central nervous system disorders
Bronchogenic carcinoma	Viral pneumonia	Encephalitis (viral or bacterial)
Carcinoma of the duodenum	Bacterial pneumonia	Meningitis (viral, bacterial, tuberculous, and fungal)
Carcinoma of the pancreas	Pulmonary abscess	Head trauma
Thymoma	Tuberculosis	Brain abscess
Carcinoma of the stomach	Aspergillosis	Brain tumors
Lymphoma	Positive pressure breathing	Guillain-Barré syndrome
Ewing's sarcoma	Asthma	Acute intermittent porphyria
Carcinoma of the bladder	Pneumothorax	Subarachnoid hemorrhage or subdural hematoma
Prostatic carcinoma	Mesothelioma	Cerebellar and cerebral atrophy
Oropharyngeal tumor	Cystic fibrosis	Cavernous sinus thrombosis
Carcinoma of the ureter		Neonatal hypoxia
		Hydrocephalus
		Shy-Drager syndrome
		Rocky Mountain spotted fever
		Delirium tremens
		Cerebrovascular accident (cerebral thrombosis or hemorrhage)
		Acute psychosis
		Peripheral neuropathy
		Multiple sclerosis

Drugs associated with hyponatremia

Vasopressin analogs

Desmopressin (DDAVP)
Oxytocin

Drugs that enhance vasopressin release

Chlorpropamide
Clofibrate
Carbamazepine–oxycarbazepine
Vincristine
Nicotine
Narcotics
Antipsychotics/antidepressants
Ifosfamide

Drugs that potentiate renal action of vasopressin

Chlorpropamide
Cyclophosphamide
Nonsteroidal anti-inflammatory agents
Acetaminophen (paracetamol)

Drugs that cause hyponatremia by unknown mechanisms

Haloperidol
Fluphenazine
Amitriptyline
Thioradazine
Fluoxetine
Sertraline

In Brief:

It caused by problems in the brain, ether infection, tumors, encephalitis, meningitis, meningioencephalitis, any hemorrhage "subdural, epidural, subarachnoid" or problems in the lung ether pneumonia, pneumonitis, lung abscess or lung tumors, and some drugs)

Acute hyponatremia:

After surgery (mostly) and aneasthesia (in up to 5% of patients).

↑ ADH because of non-osmolar stimuli: Pain
Nausea
Narcotics

1. During TUR-P.
2. Schizophrenia patients with severe compulsive water drinking (>14L/day).
3. Infusion of oxytocin and cyclophosphamide.

Chronic hyponatremia: *caused by*

- Thiazides
- Chlorpropamide
- Carbamazepine
- NSAIDs

Management :

If you want to correct hyponatremia, you have to correct it slowly by a formula.

$$\text{Sodium deficit} = (\text{desired serum } Na^+ - \text{current serum } Na^+) \times \text{TBW}$$

$$\text{Water excess} = 1 - \left[\frac{\text{Measured } Na^+}{\text{Desired } Na^+}\right] \times \text{TBW}$$

TBW = Body Weight × 0.6
TBW =40L in 70 Kg

At first, don't rise Na^+ by more than 0.5 mmol/hour or maximum 15 mmol/day.

If you give the pt more than that quickly, he might die because of central pontine myelinolysis.

For example,

If a pt with Na^+ of 110 mmol/L, and we want to raise it to 120 mmol/L (maximum 15 mmol/L), we have to calculate the total body Water which is 60% of total body weight, so we multiply 0.6 by total body weight, if the pt weight is 70, so we get about 40 L total body water, and we want to raise it 10 mmol/L so we multiply 40 by 10 to get 400 mmol of sodium to raise it from 110 to 120, giving it by hypertonic saline, not by normal saline.

Normal saline contain 150 mmol of Na^+, while hypertonic saline 3% contain 517 mmol.

To give that pt 400 mmol Na^+ is by dividing the quantity of hypertonic saline by 24. So, nearly, we give about 50 cc of hypertonic saline over 24 hours.

Treatment :

We add ½ of deficit slowly e.g. Na^+ =110. So, you must add ½ mmol/hrs not more than 15mmol/day if not, patient may die by central pontine myelilolysis.

e.g. 40 ×10 “desired-measure” = 400 mmol of Na^+

We have hypertonic saline contain 517mmol giving in 24hrs. So, we divide it by 24.

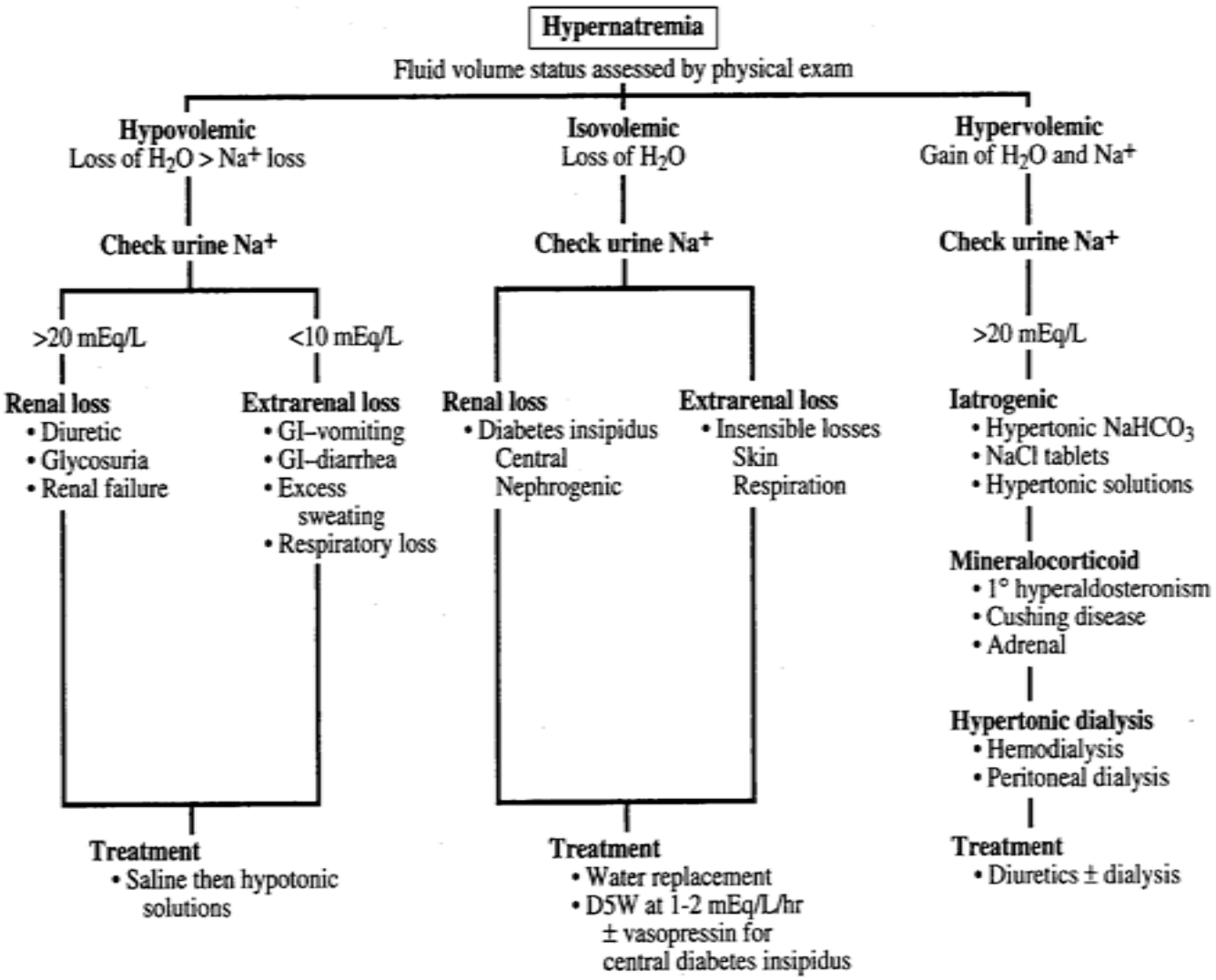
(↑Na^+) HYPERNATREMIA (↑Na^+)

All hypernatremia are real. There is no pseudohypernatremia because all forms of hypernatremia are associated with hypertonicity.

$$\text{Water deficit} = \left[\frac{\text{Measured } Na^+}{\text{Desired } Na^+}\right] - 1 \times \text{TBW}$$

Clinical features: Irritability, hyperreflexia, ataxia, & seizures.

Diagnosis and Management:



We also classify it according to volume to hypovolemic, hypervolemic or normovolemic.

As we calculate the sodium deficit in hyponatremia, we calculate water deficit for hypernatremia, because the pt is having sodium but the he needs water.

We decrease the Na^+ to the upper limit of normal range (145 mmol/L) slowly e.g. if we have a pt with Na^+ of 160 mmol/L, our target is 145 ,so the difference is 15mmol/L.)

We give it over 48 hours, half of it in the first day and the other half is in the other day, to prevent cerebral edema.

So, the Treatment for Hypernatremia:

- Adding H_2O deficit not Na^+.
- Reducing Na^+ to upper limit of normal (145 mmol).
- [160/145] – 1 × TBW = 4 L of H_2O.
- Giving ½ of it in 1st 24 hrs & the rest in the next 24 hrs. If not done like that patient may die by cerebral edema
- Remember not to forget the loss by other cause “e.g. urine” need to be added.

.: The End :.

Done By : Nephro Team

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